IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	Berndl et al.	Docket No.:	49860
Application No.:	09/937,313	Examiner:	YOUNG
Filed:	9/24/2001	Art Unit:	1618
Customer No.:	26474	Confirmation No.:	8414

For: Solubilizing aids in powder form for solid pharmaceutical presentation forms

Honorable Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

PRE-APPEAL BRIEF REQUEST FOR REVIEW

Applicants request review of the final rejection of May 28, 2008, in the above-identified application. No amendments are being filed with this request. This request is being filed with a notice of appeal. The review is requested for the reasons stated on the attached sheets.

Please charge any shortage in fees due in connection with the filing of this paper, including Extension of Time fees, to Deposit Account 14.1437. Please credit any excess fees to such account.

Regarding the Status of the Claims:

Claims 10 – 12, 14 – 18, and 20 – 24 are pending.

Claims 1 – 9, 13, 19, and 25 – 28 are canceled.

No claims have been withdrawn from consideration.

Allowable Claims:

I. Claims 10 – 12, 14 – 18, 20 and 22 – 24 are allowable in view of:
   - 35 U.S.C §103(a),
   - US 4,127,422 to Guzi Jr. et al. (hereinafter, "Guzi"),
   - US 5,858,412 to Staniforth et al. (hereinafter, "Staniforth"), and
   - US 6,086,915 to Zeligs et al. (hereinafter, "Zeligs").

II. Claims 10, 15, 16, 18, 20 and 21 are allowable in view of:
   - 35 U.S.C §103(a),
   - US 6,066,334 to Kolter et al. (hereinafter, "Kolter"),
   - Staniforth, and
   - Zeligs.

Regarding I:

Applicants respectfully submit that claims 10 – 12, 14 – 18, 20 and 22 – 24 are allowable in view of 35 U.S.C §103(a), Guzi, Staniforth, and Zeligs.

The process of independent claim 10 comprises either spray-drying a solution comprising the surface-active substance and the pharmaceutically acceptable polymer,[1] or processing the polymer and the surface-active substance in an extruder to obtain a homogeneous melt[2] and subsequently converting the melt into the free-flowing powder.[3] Similarly, the process of independent claim 22 comprises producing the free-flowing powder excipient by one of: spray-drying a solution comprising the surface-active substance and the pharmaceutically acceptable polymer,[4] or extruding the polymer and

[1] Specification, page 3, lines 31 – 37.
[2] Specification, page 3, line 44 – page 4, line 2, and Example 2.
[3] Specification, page 4, lines 4 – 11, lines 20 – 21, and Example 2.
[4] Specification, page 3, lines 31 – 37.

the surface-active substance to obtain a homogeneous melt[5] and subsequently converting the melt into the free-flowing powder.[6] Applicants respectfully submit that a combination of Guzi, Staniforth, and Zeligs would fail to meet this claim requirement. The combination of Guzi, Staniforth, and Zeligs would involve spray-drying a dispersion with a high content of solids. Guzi requires 55 – 80 % of a pigment. The water-insoluble pigment is dispersed in an aqueous medium together with a surface-active substance and a polymer. This dispersion is dried by a spray-drying process. See column 5, lines 23 – 49 of Guzi.

Furthermore, independent claim 10 relates to a process for producing an excipient that must consist essentially of a pharmaceutically acceptable polymer, and from 10 to 50% by weight, based on the total weight of said excipient, of a liquid or semisolid solubilizing surface-active substance.[7] Similarly, independent claim 22 relates to a process for producing a free-flowing powder excipient for use in a solid pharmaceutical dosage form.[8] The free-flowing powder excipient produced according to the process must consist essentially of a pharmaceutically acceptable polymer, and from 10 to 50% by weight, based on the total weight of the excipient, of a liquid or semisolid solubilizing surface-active substance.[9]

"The transitional phrase 'consisting essentially of' limits the scope of a claim to the specified materials or steps 'and those that do not materially affect the basic and novel characteristic(s)' of the claimed invention."[10] The Advisory Action of November 17, 2008, misconstrues the law, stating, "the language consisting essentially [of] only removes components that fundamentally change the resulting composition. The composition of the '422 patent remains an excipient, within the same field of endeavor as the instant claims."[11]

Applicants respectfully submit high amounts of solid pigment particles, as required by Guzi, are excluded by the transitional phrase "consisting essentially of." As

[5] Specification, page 3, line 44 – page 4, line 2, and Example 2.
[6] Specification, page 4, lines 4 – 11, lines 20 – 21, and Example 2.
[7] Specification, page 2, lines 9 – 14.
[8] Specification, page 1, lines 1 – 2.
[9] Specification, page 2, lines 9 – 14.
[10] MPEP §2111.03, citing *In re Herz*, 537 F.2d 549, 551-52, 190 USPQ 461, 463 (CCPA 1976) (emphasis added).
[11] Page 2, lines 5 – 7 of the Advisory action mailed November 17, 2008 (emphasis added).

has been explained in the Declaration under 37 C.F.R. §1.132 of Dr. Kolter, filed on October 28, 2008, the high amounts of pigments required by Guzi would materially affect the basic and novel characteristics of the claimed invention. More specifically, Guzi requires 55 – 80 % by weight of a pigment. The water-insoluble pigment of Guzi is dispersed in an aqueous medium together with a surface-active substance and a polymer. The dispersion is dried by a spray-drying process. As expressed in the Kolter declaration, "[s]ince the spray-dispersion [of Guzi] contains such a high amount of solid pigment particles spray-drying is not considered as a problem by a skilled expert."

Applicants respectfully submit, therefore, that the high amounts of pigment required by Guzi would materially affect the basic and novel characteristics of the claimed invention. As expressed on pages 1 and 2 of the specification, adding more than 10% by weight of a liquid or semisolid solubilizing surface-active substance to a polymeric carrier was expected to cause processability problems, because of the waxy consistency of the resultant formulation. This expectation is also expressed on page 2 of the enclosed Declaration under 37 C.F.R. §1.132 by Dr. Karl Kolter, which states,

> [l]iquid and semi-solid surface-active substances and pharmaceutical formulations comprising such substances are often difficult to handle because of the wax-like and sticky consistency of the masses. These surface-active substances also have a plastifying effect. Especially in case of formulation mixtures for direct compression to tablets such surface-active substances have hitherto caused problems.

Applicants respectfully submit, therefore, that the high amounts of pigment required by Guzi would materially affect the basic and novel characteristics of the claimed invention.

Moreover, "[a] greater than expected result is an evidentiary factor pertinent to the legal conclusion of obviousness ... of the claims at issue."[12] Similarly, "[a]bsence of property which a claimed invention would have been expected to possess based on the teachings of the prior art is evidence of unobviousness."[13] Such is the case with the present invention. As further declared by Dr. Kolter,

[12] MPEP §716.02(a), citing *In re Corkill*, 711 F.2d 1496, 226 USPQ 1005 (Fed. Cir. 1985).
[13] MPEP §716.02(a), citing *Ex parte Mead Johnson & Co.* 227 USPQ 78 (Bd. Pat. App. & Inter. 1985).

> [i]t was unexpected that the excipients obtained either by spray-drying or by melt extrusion turned out to be free-flowing powders that can easily be processed without restriction to give solid dosage forms. Furthermore it was unexpected that the excipients could be processed by spray drying. An ordinarily skilled expert would certainly have expected that especially spray-drying of a solution of the two specific components in the claimed amounts would not work at all because of the plastifying properties of the surface-active substances.

In light of what a person of ordinary skill in the art would have expected, Examples 1 – 3 provide evidence of unexpected results that are commensurate in scope with the claimed invention, and establish the non-obviousness thereof. Applicants respectfully assert, "[t]he ultimate determination of patentability must be based on consideration of the entire record, by a preponderance of evidence, with due consideration to the persuasiveness of any arguments and any secondary evidence."[14] Since the Office action fails to consider the unexpected results presented in the specification, a proper determination of patentability has not been made.

Finally, the Kolter declaration explains that a skilled artisan had no apparent reason to make the proposed combination at all. The references are in a different fields of endeavor and would not have logically commended themselves to the attention of a person of ordinary skill in the art, when trying to solve the problem addressed by the present invention. As expressed in the declaration, a skilled artisan would not have looked to these references for guidance.

Regarding II:

Applicants respectfully submit that claims 10, 15, 16, 18, 20 and 21 are allowable in view of 35 U.S.C §103(a), Kolter, Staniforth, and Zeligs.

Applicants respectfully submit that the proposed combination would require from 10 – 95% by weight of polyvinylacetate, as described by Kolter. At column 2, lines 57 – 60, Kolter explains that the polyvinyl acetate is not miscible with the N-vinylpyrrolidone-containing polymer. At column 2, lines 56 – 57, Kolter explains that polyvinyl acetate

[14] MPEP §716.01(d), citing *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992).

markedly increases the plasticity in the final product.

The 10 – 95 % by weight of polyvinyl acetate required by Kolter is excluded by independent claim 10, which relates to a process for producing an excipient that must consist essentially of a pharmaceutically acceptable polymer, and from 10 to 50% by weight, based on the total weight of said excipient, of a liquid or semisolid solubilizing surface-active substance.[15] As expressed in the Kolter Declaration, "[i]mproving the processability of the excipient with regard to stickiness is of no concern to Kolter et al., since this problem does not occur due to the essentially different composition and morphology of the binder."

Claims 15, 16, 18, 20 and 21 depend from claim 10.

In Conclusion:

Favorable action is respectfully requested. In order to facilitate the resolution of any issues or questions presented by this paper, please feel free to contact the undersigned by phone to further the discussion.

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[15] Specification, page 2, lines 9 – 14.